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SYNTHESIS AND PROPERTIES OF DITHIOACETALS OF CONFORMATIONALLY CONSTRAINED α-ACYL-β-AMINOVINYL KETONES OF THE 8-AZASTEROID

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We have studied the reaction of α-acyl-β-aminovinyl ketones of the 8-azasteroid series with ethanedithiol. The occurrence and orientation of the reaction are determined by structural and steric factors. As applied to derivatives of 8-azasteroids of the D-homo series, the reaction is irreversible and consequently the dithioacetal derivatives of this series are easily hydrolyzed under acid and base conditions. Desulfurization over Raney nickel of the 17-dithioacetal derivative of 8-azagona-12,17-dione occurs with simultaneous dehydrogenation of the C ring and leads to the 17-deoxo-9,11-dehydro derivative, while desulfurization of the 1-dithioacetal of 8-aza-D-homogona-12,17-a-dione leads to the 12-deoxo derivative. By reaction of the 12-dithioacetal of 8-aza-D-homogona-17a-one with hydroxylamine, we obtained the 12-oximino derivative, which is the result of an unusual reaction at the site of the spiro coupling of the dithiolane ring with the 8-azasteroid ring.

Investigations in the area of heterocyclic analogs of steroids (in which series the 8-azasteroids occupy a significant position) have been the subject of steadfast attention from many specialists [1-3]. Despite the fact that compounds of this type are not observed in nature, interest in them is due to the biological activity they display (anti-inflammatory, immunotropic, etc.) [4-7]. It is also important that compounds of this class are generally devoid of hormonal effects, a very important attribute of the physiological action of steroidal hormones and their synthetic analogs [8].

The simplest and most effective approach to compounds of this series is the reaction of annellation of cyclic Schiff bases, such as 3,4-dihydrodroisoquinolines I with 2-acylcycloalkane-1,3-dones II, making it possible in one step to form the ABCD-tetracyclic 8-azasteroid skeleton III [3, 9]. We should especially note that annelation occurs with exceptionally high regio- and stereoselectivity [10, 11]. So far a broad series of the named compounds have been obtained using this method, and some of their physicochemical [10-13] and biological [5-7] properties has been studied. Further development of the investigations is viewed as involving goal-directed skeletal and functional transformations.

The key structural element of compounds in the considered series is the $N_{(8)}-C_{(14)} = C_{(13)}(-C_{(12)} = O)-C_{(17,17a)} = O$ α-acyl-β-aminovinylcarbonyl (AAVC) moiety, the properties of which are still insufficiently studied. Nevertheless, available data [3, 9-16] allow us to hypothesize that the most promising direction for functional transformations of the indicated moiety are nucleophilic reactions at the carbonyl group of the AAVC moiety.

We know [17-20] that 1,2- and 1,3-dimercaptans are widely used in synthesis of dithioacetal derivatives in transformations of carbonyl compounds. Earlier [19, 20], dithiolane derivatives were successfully used in transformations of 12-keto- and 12,17-diketo-8-aza-16-oxasteroids. At the same time, attempts to obtain dithiolane derivatives in the 12,17a-diketo-8-aza-17-oxa-D-homogonane series proved to be unsuccessful [20]. In a preliminary report [21], we showed that reaction of 8-aza-D-homogona-1,3,5(10),13-tetraene-12,17a-dione (IIIb) with ethanedithiol leads to a mixture of regiomeric dithiolane derivatives IVb and Vb.

With the goal of studying the possibility of transformation of the AAVC moiety of 8-azasteroids IIIa-f and on their basis searching for new biological active compounds, we have studied the reaction of the latter with ethanedithiol. On the other hand, it seemed of interest to experimentally test some earlier statements: a) the empirical rule for conjugation configurations in [14],

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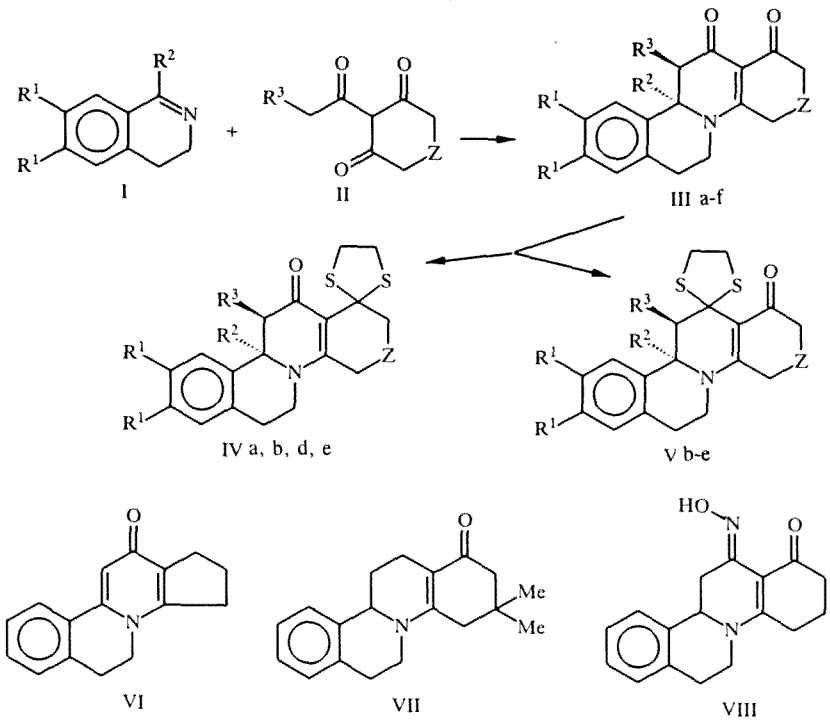
according to which in the AAVC series and related cross-coupled donor–acceptor compounds only one of two theoretically possible conjugation configurations are realized; b) claims about electronic tautomerism of such systems, defined as "mesomeric tautomerism" [15, 16].



III a-d, f, IVa, b d Vb–d R^1 = H; III, IV, Ve R^1 = OMe; III a–c, e, f, IVa, b, e, Vc R^2 = H; III, IV, Vd R^2 = Me; III a–d, IVa, b, d Vb–d R^3 = H; III, IV, Vd R^3 = Me; IIIe R^3 = Et; IIIa, IVa Z = –; III, IV, Vb, d e, Z = CH_2; IIIc, f Vc Z = CMe_2

As the starting compounds, we used the previously described 8-azagonane (IIIa) [9] and 8-aza-D-homogonanes IIIb-f [9, 11, 22, 23]. The application of familiar synthesis methods for dithiolane derivatives [17-20] to 8-azasteriods IIIa-f did not give the desired result. This probably was due on the one hand to the instability of the latter toward the action of strong proton-donor acids at elevated temperatures, and on the other hand to the fact that in catalysis by Lewis acids (boron trifluoride etherate), coordination of the latter occurs at the nitrogen atom, which excludes activation of the carbonyl groups. At the same time, we observed that carrying out the reaction in trifluoroacetic acid at ~20°C makes it possible to obtain the dithioacetals IVa, b, d, e and Vb-e. We should note that exclusively the 17-dithiolane derivative IVa is formed from 8-azagonane (IIIa), while only the 12-dithiolane derivative Vc is formed from the 8-aza-D-homogonane with a gem-dimethyl group a $C_{(16)}$ (IIIc). We obtained both the derivatives IVb, d, e and Vb, d, e from 8-aza-D-homogonanes IIIb, d, e, while we did not detect formation of any dithiolane derivatives from 8-aza-D-homogonane IIIf even when holding the reaction mixture for 30 days. Such a result indicates a determining role for structural and steric factors in the occurrence and orientation of the reaction. We should especially note that, except for 8-azagonane (IIIa), undergoing full conversion to the derivative IVa, none of the studied examples could be made to react with complete consumption of the starting compound; i.e., in this case, in contrast to the previously described case in [19, 20], the reaction has the character of an equilibrium, and the derivatives IVb-e and Vb-e are unstable and may be hydrolyzed to the starting materials.

The structure of the compounds obtained was confirmed by physicochemical analysis data and some conversions. Thus in the IR spectra of thioketals IVa, b, d, e, there are absorption bands characteristic for stretching vibrations of the cis-s-trans β-aminovinylcarbonyl $N_{(8)}–C_{(14)} = C_{(13)}–C_{(12)} = O$ (AVC) moiety at 1565 cm^{-1} for IVa and 1527-1518 cm^{-1} for Vb, d, e [24], while for the thioketals Vb-e we observe bands characteristic for stretching vibrations of the trans-s-trans AVC $N_{(8)}–C_{(14)} = C_{(13)}–C_{(17a)} = O$ moiety at 1550-1524 cm^{-1} [24]. The high-frequency shift of the absorption band for compound IVa compared with compounds IVb, d, e probably is due to structural differences: the six-membered D rings in compounds IVb, d, e and the five-membered D ring in compound IVa.

TABLE 1. Characteristics of 8-Azasteroid Derivatives IVa, b, d, e, Vb-e, VIII

Compound	Empirical formula	T_{mp}, °C (with decomp.)	IR spectrum* (KBr, ν, cm^{-1})	UV spectrum (ethanol, λ_{max}, nm, log ε)	Yield, %
IVa	$C_{18}H_{19}NOS_2$	239-241.5	1633 s, 1609 w, 1587 m, 1565 vs, 1495 w, 1478 m, 1422 w, 1356 m, 1289 m, 1197 m, 752 m,	325 (4,12)	81,8
IVb	$C_{19}H_{21}NOS_2$	232-234	1635 s, 1521 vs, 1496 m, 1289 m, 1260 w, 1187 m, 767 m, 755 m,	210 (4,11), 329 (4,06)	56,5
IVd	$C_{20}H_{23}NOS_2$	229-231.5	1641 s, 1615 shldr, 527 vs, 1496 m, 1447 m, 1430 shldr, 1325 w, 1295 w, 1180 m, 1165 w, 1047 m, 1042 w, 775 m,	331 (4,01)	47,5
IVe	$C_{22}H_{27}NO_3S_2$	188-190	1642 s, 1620 w, 1518 vs, 1455 m, 1370 w, 1330 w, 1262 s, 1221 m, 1126 w, 1019 w,	202,7 (4,82), 228,5 (4,29), 326,8 (4,21), 389,7 (3,86)	43,1
Vb	$C_{19}H_{21}NOS_2$	199-200.5	1627 m, 1528 vs, 1498 m, 1435 m, 1417 m, 1308 m, 1287 m, 1198 m, 778 m,	200 (4,25), 309 (4,40)	39,6
Vc	$C_{21}H_{25}NOS_2$	182-183.5*2	1645 m, 1550 s, 1530 shldr, 1412 m, 1321 m, 1280 m, 774 m, 748 m,	310 (4,41)	65,0
Vd	$C_{20}H_{23}NOS_2$	208-212*2	1624 m, 1524 vs, 1492 w, 1440 m, 1424 m, 1370 w, 1335 m, 1312 w, 1197 m, 1165 w, 780 w,	237 (3,55), 308 (4,34)	33,5
Ve	$C_{22}H_{27}NO_3S_2$	212-214*2	1634 s, 1610 w, 1530 vs, 1512 vs, 1435 s, 1420 m, 1336 s, 1307 s, 1264 s, 1251 s, 1220 s, 1204 m, 1190 s, 1129 s, 1095 w, 1020 w, 1006 w, 860 w, 772 m,	235 (3,66), 307 (4,09)	31,1
VIII	$C_{17}H_{18}N_2O_2$	190-191	3215 vs, 1630 s, 1515 vs, 1492 s, 1418 s, 1362 s, 1342 s, 1320 m, 1288 w, 1225 w, 1190 s, 1165 m, 1065 m, 1020 m, 934 s, 764 m,	207 (4,45), 263 (4,31), 319 (4,38)	92,9

*Relative intensities of absorption and shape of the signal: vs) 95-75%; s) 75-55%; m) 55-35%; w) 35-15%; shldr) shoulder,

*2Without decomposition.

The electronic absorption spectra have no less characteristic a form. Thus the dithiolane derivatives Vb-e are characterized by an intense absorption band at 307-310 nm and the derivatives IVa, b, d, e are characterized by an intense band at 325-331 nm, which is quite consistent with electronic spectra of the corresponding 8-azasteriods also having cis-s-trans and trans-s-trans AVC moieties [25].

In the mass spectra of the thioacetals IVa, b, d, e and Vb-e, we observe molecular ion peaks and also intense [M + 2] ion peaks characteristic for sulfur-containing organic compound [26].

In the PMR spectra of the dithioacetals IVa, b, d, e and Vb-e, along with the resonance signals from protons of the 8-azasteriods skeleton, there are resonance signals from protons of the methylene groups of the dithiolane ring (Tables 1 and 2).

According to spectral studies and comparison of the constants, desulfurization of the dithioacetal IVa over Raney nickel under the conditions of the method in [20, 27] gave (instead of the expected cis-s-trans β-aminovinyl ketone) the γ-pyridone derivative VI, obtained earlier in [28] as a result of a two-step procedure of dehydrogenation–ionic hydrogenation of 8-azagona-12,17-dione. An explanation for such an unexpected result (dehydrogenation over Raney nickel) may be the reduced stability of the cis-s-cis AVC moiety with the annellated five-membered D ring. Desulfurization of dithioacetal Vc led to the previously described [28] trans-s-trans β-aminovinyl ketone VII.

TABLE 2. PMR Spectra of Compounds IVa, b, d, e, Vb-e, VIII in $CDCl_3$

Compound	Chemical shifts, δ, ppm (J, Hz)
IVa	2,50 (1H, t, $C_{(11)}H_B$; 16,0), 2,61...2,90 (6H, m, $C_{(11)}H_A$, $C_{(15)}H_2$, $C_{(6)}H_e$, $C_{(16)}H_2$), 3,10 (1H, d.d.d., $C_{(6)}H_a$; 15,0, 11,0, 4,5), 3,22...3,40 (3H, m, $C_{(7)}H_a$, CH_2S), 3,67...3,88 (3H, m, $C_{(7)}H_e$, CH_2S), 4,82 (1H, d.d., $C_{(9)}H_X$; 16,0, 4,5), 7,12...7,28 (4H, m, $C_{(1)}$...$C_{(4)}$H arom.)
IV b	1,85...2,06 (2H, m, $C_{(16)}H_2$), 2,10...2,19 (1H, m, $C_{(17)}H$), 2,26...2,46 (2H, м, $C_{(15)}H$, $C_{(17)}H$), 2,49 (1H, t, $C_{(11)}H_B$; 16,0), 2,54...3,17 (4H, m, $C_{(6)}H_a$, $C_{(6)}H_e$, $C_{(6)}H_a$, $C_{(15)}H$), 2,73 (1H, d.d., $C_{(11)}H_A$; 4,0, 16,0), 3,23...3,46 (2H, m, CH_2S), 3,62...3,75and 3,96...4,16(3H,m,$C_{(7)}H_e$, CH_2S), 4,69 (1H, d.d., $C_{(9)}H_X$; 4,0, 16,0), 7,08...7,32 (4H, m, $C_{(1)}$...$C_{(4)}$H arom).
IV d	1,65 (3H, s, $C_{(9)}CH_3$), 1,99 (3H, m, $C_{(16)}H_2$, $C_{(17)}H$), 2,34 (2H, m, $C_{(15)}H$, $C_{(17)}H$), 2,45 (1H, m, $C_{(15)}H$), 2,60 (1H, m, $C_{(11)}H_B$; 16,0), 2,70 (1H, d, $C_{(11)}H_A$; 16,0), 2,86 (1H, d.d.d., $C_{(6)}H_e$; 4,0, 12,0, 14,0), 3,08 (1H, d.d.d., $C_{(6)}H_a$; 4,0, 12,0, 12,0), 3,36 (3H, m, $C_{(7)}H_a$, CH_2), 3,64 (1H, m, CH_2S), 4,04 (2H, m, $C_{(7)}H_e$, CH_2S), 7,10...7,30 (4H, m, $C_{(1)}$...$C_{(4)}$H arom.)
IV e	0,71 (3H, d, $C_{(11)}CH_3$; 7,5), 1,96...2,16 (2H, m, $C_{(16)}H_2$), 2,32 (2H, m, $C_{(17)}H_2$), 2,50 (1H, d.d.d.d., $C_{(11)}H$; 3,5, 7,5, 7,5, 7,5), 2,64 (2H, m, $C_{(15)}H_2$), 2,72 (1H, t. t, $C_{(6)}H_e$; 3,0, 3,0, 12,0), 2,95 (1H d.d.d., $C_{(6)}H_a$; 12,0, 12,0, 3,0), 3,09 (1H, d.d., d $C_{(7)}H_a$; 3,0, 12,0, 12,0), 3,23...3,46 (2H, m, CH_2S), 3,68 (1H, m, CH_2S), 3,84 (3H, s, OCH_3), 3,88 (3H, s, OCH_3), 4,06 (2H, m, $C_{(7)}H_e$, CH_2S), 4,74 (1H, d, $C_{(9)}H$; 3,5), 6,55 (1H, s, arom.), 6,63 (1H, s, H arom.)
V b	1,98 (2H, m, $C_{(16)}H_2$), 2,16...2,54 (3H, m, $C_{(15)}H$, $C_{(17)}H_2$), 2,44 (1H, d.d., $C_{(11)}H_B$; 11,0, 14,0), 2,65 (1H, t.t. $C_{(15)}H$; 4,0, 4,0, 16,0), 2,79 (1H, d.d., $C_{(11)}H_A$; 2,5, 14,0), 2,81 (1H, t.t. $C_{(6)}H_e$; 4,0, 11,0, 11,0), 2,99 (1H, d.d.d., $C_{(6)}H_a$; 4,0, 11,0, 11,0), 3,20 (1H, d.d.d., $C_{(7)}H_a$; 12,0, 11,0, 4,0), 3,34...3,51 (2H, m, CH_2S), 3,65 (1H, m, CH_2S), 4,05 (1H, t.t. $C_{(7)}H_e$; 4,0, 4,0, 12,0), 4,16 (1H, m, CH_2S), 4,71 (1H, d.d., $C_{(9)}H_X$; 2,5, 11,0), 7,12...7,35 (4H, m, $C_{(1)}$...$C_{(4)}$H arom.)
V c	1,06 (3H, s, $C_{(16)}CH_3$), 1,10 (3H, s, $C_{(16)}CH_3$), 2,24 (2H, s, $C_{(17)}CH_2$), 2,38 (2H, s, $C_{(15)}CH_2$), 2,41 (1H, d.d., $C_{(11)}H_B$; 9,0, 11,0), 2,79 (1H, d.d., $C_{(11)}H_A$; 2,0, 11,0), 2,81 (1H, t.t. $C_{(6)}H_e$; 2,5, 2,5, 12,0), 2,99 (1H, d.d., $C_{(6)}H_a$; 2,5, 12,0, 12,0), 3,19 (1H, d.d.d., $C_{(7)}H_a$; 2,5, 12,0, 12,0), 3,32...3,52 (2H, m, CH_2S), 3,61 (1H, m, CH_2S), 4,04 (1H, t.t. $C_{(7)}H_e$; 2,5, 2,5, 12,0), 4,15 (1H, m, CH_2S), 4,68 (1H, d.d., $C_{(9)}H_X$; 2,0, 9,0), 7,11...7,32 (4H, m, $C_{(1)}$...$C_{(4)}$H arom.)
V d	1,72 (3H, s, $C_{(9)}CH_3$), 1,99 (2H, m, $C_{(16)}H_2$), 2,40 (4H, m, $C_{(15)}H_2$, $C_{(17)}H_2$), 2,64 (1H, d, $C_{(11)}H_B$; 14,5), 2,78 (1H, t.t. $C_{(6)}H_e$; 4,5, 4,5, 16,0), 2,98 (1H, d, $C_{(11)}H_A$; 14,5), 2,99 (1H, d.t.d., $C_{(6)}H_a$; 4,5, 12,0, 16,0), 3,06 (1H, d.d.d., $C_{(7)}H_a$; 4,5, 12,0, 12,0), 3,30...3,52 (3H, m, CH_2S), 3,96 (1H, m, CH_2S), 4,10 (1H, t.t. $C_{(7)}H_e$; 4,5, 4,5, 12,0), 7,07...7,30 (4H, m, $C_{(1)}$...$C_{(4)}$H arom.)
V e	0,88 (3H, d, $C_{(11)}CH_3$; 6,5), 1,96 (2H, m, $C_{(16)}H_2$), 2,32 (1H, d.d.d.d., $C_{(11)}H$; 1,5, 6,5, 6,5, 6,5), 2,35...2,52 (4H, m, $C_{(15)}H_2$, $C_{(17)}H_2$), 2,67 (1H, t.t. $C_{(6)}H_e$; 2,5, 2,5, 16,0), 2,90 (1H, d.t.d., $C_{(6)}H_a$; 2,5, 12,0, 16,0), 3,10 (1H, d.d.d., $C_{(7)}H_a$; 2,5, 12,0, 12,0), 3,35...3,45 (2H, m, CH_2S), 3,60 (1H, m, CH_2S), 3,88 (3H, s, OCH_3), 3,90 (3H, s, OCH_3), 4,12 (1H, t.t. $C_{(7)}H_e$; 2,5, 2,5, 12,0), 4,26 (1H, m, CH_2S), 4,98 (1H, d, $C_{(9)}H$; 1,5), 6,61 (1H, s, CH arom.), 6,66 (1H, s, CH arom.)
VIII	1,96...2,05 (2H, m, $C_{(16)}H_2$), 2,32 (2H, m, $C_{(17)}H_2$), 2,38 (1H, d.d., $C_{(11)}H_B$; 12,0, 16,0), 2,60 (2H, m, $C_{(15)}H_2$), 2,90 (1H, t.t. $C_{(6)}H_e$; 4,0, 4,0, 15,5), 3,05 (1H, d.t. d, $C_{(6)}H_a$; 4,0, 12,0, 15,5), 3,35 (1H, d.d.d., $C_{(7)}H_a$; 4,0, 12,0, 14,0), 4,07 (1H, d, d, $C_{(11)}H_A$; 4,5, 16,0), 4,12 (1H, t.t. $C_{(7)}H_e$; 4,0, 4,0, 14,0), 4,61 (1H, d.d., $C_{(9)}H_X$; 4,5, 12,0), 7,13...7,37 (1H, m, $C_{(1)}$...$C_{(4)}$H arom.)

The above hypothesis about the possibility of hydrolytic cleavage of the dithioacetals obtained has been experimentally confirmed by hydrolysis of the dithioacetals IVb, e and Vc, e to the starting 8-aza-D-homogona-12,17a-diones IIIb, c, e, equally efficiently accomplished by both acid and base catalysis. This result is probably a consequence of stereoelectronic factors, due to the geminal carbonyl group. On the other hand data on the hydrolysis of dithioacetals provides a basis for hypothesizing that attack by nucleophilic agents, contrary to commonly held opinions, in this case should be directed not at the carbonyl group but rather at the site of spiro coupling of the dithiolane ring with the 8-azasteroid ring. This hypothesis was confirmed by reaction of dithioacetal Vb with hydroxylamine, as a result of which the 17a-keto-12-oximino derivative VIII was synthesized.

Thus the results obtained show that when using 8-azagonane IIIa and 8-aza-D-homogonane IIIc, the reaction is accomplished exclusively regioselectively and leads to 17- and 12-dithioacetals IVa and Vc respectively. In the case of the sterically hindered 8-aza-D-homogonane IIIf the reaction does not occur; but with 8-aza-D-homogonanes IIIb, d, e, the reaction occurs both at the $C_{(12)}$ and $C_{(17a)}$ carbonyl groups, with some preference for the $C_{(17a)}$ dithioacetal regiomers (Table 1). These results raise doubts concerning the conclusion that a specific preferred conjugation configuration is realized in the 8-azasteroid AAVC series [14], and (albeit indirectly) indicate an equivalence of the carbonyl groups of the AAVC moiety, consistent with the claim of electronic tautomerism for such systems in [15, 16]. The dithioacetal derivatives IVb, d, e and Vb-e obtained are

not very stable and may be easily hydrolyzed to the starting compounds or converted to other compounds (such as the oximino derivatives) as a result of reaction with nucleophilic agents. On the other hand, desulfurization of the dithioacetals obtained is a rather convenient approach to the corresponding deoxo derivatives VI and VII. The elevated lability and consequently the associated reactivity of the dithioacetal derivatives of the 8-aza-D-homogonane series certainly is connected with the effect of the adjacent carbonyl group, indicating specificity of these derivatives.

EXPERIMENTAL

The course of the reactions and the purity of the derivatives obtained were monitored using TLC on Silufol UV-254 plates, 19:1 chloroform-methanol as the eluent, visualization in UV light or with iodine vapors. The reaction products were isolated chromatographically on silica gel. The melting points were determined on a Boetius heating stage. The IR spectra were obtained on a UR-20 in KBr pellets. The electronic spectra were taken on Specord UV-vis spectrometer in ethanol solutions; the PMR spectra were taken on a Bruker AC-200 (200 MHz) in CCl_3 with TMS as the internal standard, digital resolution 0.5 Hz. The mass spectra were recorded on a Varian MAT-311 spectrometer, ionizing electron energy 70 eV.

The yields, melting points, IR, UV, and PMR spectroscopy and mass spectrometry data of the compounds obtained are presented in Tables 1 and 2.

17-Spiro-2′-(1′,3′-dithiolane)-8-azagona-1,3,5(10),13-tetraen-12-one (IVa, $C_{18}H_{19}NOS_2$). A mixture of 1.52 g (6 mmoles) 8-azagonane (IIIa) [9] and 0.6 ml (7 mmoles) ethanedithiol in 2 ml trifluoroacetic acid was carefully heated until homogenized and allowed to stand at ~20°C for ten days. Then the reaction mixture was quenched with potassium carbonate and extracted with chloroform. The extracts were evaporated and the residue was crystallized from a 1:2 chloroform–hexane mixture. Obtained: 1.35 g (81.8%) dithioacetal IV in the form of white crystals.

17a-Spiro-2′-(1′,3′-dithiolane)-8-aza-D-homogona-1,3,5(10),13-tetraen-12-one (IVb, $C_{19}H_{21}NOS_2$), 12-Spiro-2′-(1′,3′-dithiolane)-8-aza-D-homogona-1,3,5(10),13-tetraen-17a-one (Vb, $C_{19}H_{21}NOS_2$). A mixture of 1.34 g (5 mmoles) 8-aza-D-homogonane IIIb [9] and 0.5 ml (6 mmoles) ethanedithiol was heated until homogenized and allowed to stand at ~20°C for seven days. Then the reaction mixture was evaporated and the residue was dissolved in chloroform and treated with solid sodium bicarbonate. The filtrate obtained was chromatographed on silica gel 5/40μ, eluting with chloroform. Three fractions of eluates were collected. By crystallization of the residue of the first fraction from a 1:3 chloroform–hexane mixture, we obtained 0.97 g (56.5%) dithioacetal IVb in the form of pale green crystals. By crystallization of the residue of the second fraction from a 1:1:2 chloroform–ether–hexane mixture, we obtained 0.68 g (39.6%) dithioacetal Vb in the form of pale yellow crystals. Evaporation of the third fraction yielded 40 mg (3%) of the starting 8-aza-D-homogonane IIIb.

16,16-Dimethyl-12-spiro-2′-(1′,3′-dithiolane)-8-aza-D-homogona-1,3,5(10),13-tetraen-17a-one(Vc,$C_{21}H_{25}NOS_2$). A mixture of 1.48 g (5 mmoles) 8-aza-D-homogonane IIIc [9] and 1 ml ethanedithiol in 2.5 ml trifluoroacetic acid was held at ~20°C for five days. Then the excess ethanedithiol and acid were evaporated at reduced pressure. The residue was dissolved in chloroform, treated with solid potassium carbonate, and filtered. The filtrate was evaporated, the residue was chromatographed on silica gel 40/60μ. Two fractions of eluates were collected. By crystallization of the residue of the first fraction from a 1:1 ether–hexane mixture, we obtained 1.21 g (65.0%) dithioacetal Vc in the form of pale yellow crystals. From the second fraction after evaporation, we obtained 0.49 g (33%) of the starting 8-aza-D-homogonane IIIc.

9-Methyl-17a-spiro-2′-(1′,3′-dithiolane)-8-aza-D-homogona-1,3,5(10),13-tetraen-12-one (IVd, $C_{20}H_{23}NOS_2$), 9-Methyl-12-spiro-2′-(1′,3′-dithiolane)-8-aza-D-homogona-1,3,5(10),13-tetraen-17a-one (Vd, $C_{20}H_{23}NOS_2$). A mixture of 1.41 (5 mmoles) 8-aza-D-homogonane IIId [23] and 0.55 ml (6 mmoles) ethanedithiol in 1.5 ml trifluoroacetic acid was heated until homogenized and allowed to stand at ~20°C for six days. Then the reaction mixture was quenched with potassium carbonate, extracted with ether, and evaporated. The residue was chromatographed on silica gel 40/100μ, eluting with chloroform. Four fractions of eluates were collected. The first fraction, containing excess ethanedithiol, was discarded. By crystallization of the residue of the second fraction from a 1:1 ether–hexane mixture, we obtained 0.85 g (47.5%) dithiolane derivative IVd in the form of pale green crystals. By crystallization of the residue of the third fraction from a 1:2 chloroform–hexane mixture, we obtained 0.6 g (33.5%) dithioacetal Vd in the form of pale yellow crystals. By evaporation of the fourth fraction and crystallization of the residue from an alcohol–ether mixture, we obtained 0.27 g (19.1%) unreacted 8-aza-D-homogonane IIId.

11-Methyl-2,3-dimethoxy-17a-spiro-2′-(1′,3′-dithiolane)-8-aza-D-homogona-1,3,5(10),13-tetraen-12-one (IVe, $C_{22}H_{27}NO_3S_2$), 11-Methyl-2,3-dimethoxy-12-spiro-2′-(1′,3′-dithiolane)-8-aza-D-homogona-1,3,5(10),13-tetraen-17a-one (Ve, $C_{22}H_{27}NO_3S_2$). A mixture of 1.71 g (5 mmoles) 8-aza-D-homogonane IIIe [11] and 0.5 ml (6 mmoles) ethanedithiol in 1.5 ml trifluoroacetic acid was allowed to stand at ~20°C with periodic shaking for six days. After a day, the reaction mixture became homogeneous. Then the reaction mixture was evaporated at reduced pressure, the residue was dissolved in chloroform and then washed successively with water, 5% $NaHCO_3$ solution, and water. Then it was dried over sodium sulfate and evaporated. The residue was chromatographed on silica gel 40/100μ, eluting with a 2:1 chloroform–hexane mixture. Three fractions of eluates were collected. By crystallization of the residue of the first fraction from an ether–hexane mixture, we obtained 0.9 g (43.1%) dithioacetal IVe in the form of pale green crystals. By crystallization of the residue of the second fraction from a 1:1 chloroform–hexane mixture, we obtained 0.65 g (31.1%) dithioacetal Ve in the form of pale rose crystals. From the residue of the third fraction, we recovered 0.4 g (23.4%) of the starting 8-aza-D-homogonane IIIe.

Acid Hydrolysis of Dithioacetals. General Technique. 3-5 drops of concentrated hydrochloric acid was added to a solution of dithioacetal in 10 ml 90% aqueous ethanol and allowed to stand at ~20°C for 12-24 h. Then 1-2 ml of a saturated solution of sodium bicarbonate was added to the reaction mixture; this was evaporated and the aqueous residue was extracted with chloroform. By evaporation of the extract and crystallization of the residue from an alcohol–ether mixture, we obtained 8-azasteroid 12,17a-diketones.

From 0.34 g (1 mmole) dithioacetic IVb, we obtained 0.22 g (81%) diketone IIIb, identical to a known sample [9].

From 0.21 g (0.5 mmoles) dithioacetal Ve, we obtained 0.15 g (88%) diketone IIIe, identical with a known sample [11].

Base Hydrolysis of Dithioacetals. General Technique. 1-2 drops of a 40% solution of sodium hydroxide was added to a solution of dithioacetal in 10 ml 90% aqueous methanol and allowed to stand at ~20°C for 7-12 h. Then the reaction mixture was evaporated, diluted with a 5% solution of ammonium chloride, and extracted with chloroform. By evaporation of the extracts and crystallization of the residue from an alcohol–ether residue, we obtain 8-azasteroid 12,17a-diketones.

From 0.21 g (0.5 mmoles) dithioacetal IVe, we obtained 0.16 g (94%) diketone IIIe, identical with a known sample [11].

From 0.15 g (0.4 mmoles) dithioacetal Vc, we obtained 0.11 g (92%) diketone IIIc, identical with a known sample [9].

Desulfurization of Dithioacetal Derivatives IVa and Vc. 5 g Raney nickel was added to a solution of 0.33 g (1 mmole) dithioacetal IVa in 20 ml methanol and this was boiled for 1 h. Then the hot solution was filtered, the catalyst was washed with 10 ml hot methanol. The combined filtrates were evaporated, the residue was crystallized from a 1:5 chloroform–hexane mixture. Obtained: 0.21 g (88.6%) γ-pyridone VI in the form of white crystals. T_{mp} 249-252°C. Lit.: T_{mp} 250-252°C [28].

Raney nickel (5 g) was added to a solution of 0.5 g (1.3 mmoles) dithioacetal Vc in 20 ml methanol and this was boiled for 2 h. Then the catalyst was filtered off and it was washed with hot methanol. The combined filtrates were evaporated, the residue was crystallized from a 1:3 ethylacetate–hexane mixture. Obtained: 0.35 g (95.9%) β-aminovinyl ketone VII. T_{mp} 131-133°C. Lit.: T_{mp} 128-130°C [28].

12-Oximino-8-aza-D-homogona-1,3,5(10),13-tetraen-17a-one (VIII, $C_{17}H_{18}N_2O_2$). A solution obtained from 0.12 g (1.7 mmoles) hydroxylamine hydrochloride and 3.4 ml 0.5 M sodium methoxide solution in 10 ml methanol was added to a solution of 0.52 g (1.5 mmoles) dithioacetal Vb in 10 ml methanol. The mixture was boiled for 1.5 h and then allowed to evaporate. The residue was dissolved in chloroform, the solution was washed with water, dried over sodium sulfate, filtered, and evaporated. By crystallization of the residue from ethanol, we obtained 0.39 g (92.9%) oxime VIII in the form of white crystals.

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